United States Court of Appeals for the Federal Circuit

ALLERGAN, INC.,
Plaintiff-Appellee

v.

SANDOZ INC., LUPIN LTD., LUPIN PHARMACEUTICALS, INC., HI-TECH PHARMACAL CO., INC.,
Defendants-Appellants

2014-1275

Appeal from the United States District Court for the Eastern District of Texas in No. 6:11-cv-00441-MHS, Judge Michael H. Schneider.

Decided: August 4, 2015

JUANITA ROSE BROOKS, Fish & Richardson, P.C., San Diego, CA, argued for plaintiff-appellee. Also represented by CRAIG E. COUNTRYMAN; JONATHAN ELLIOT SINGER, DEANNA JEAN REICHEL, Minneapolis, MN; DOUGLAS E. MCCANN, SUSAN M. COLETTI, Wilmington, DE.

DEANNE MAYNARD, Morrison & Foerster LLP, Washington, DC, argued for defendant-appellant Sandoz Inc. Also represented by BRIAN ROBERT MATSUI; DAVID

CLARENCE DOYLE, ANDERS T. AANNESTAD, JAMES CEKOLA, San Diego, CA.

WILLIAM A. RAKOCZY, Rakoczy Molino Mazzochi, Siwik LLP, Chicago, IL, argued for defendants-appellants Lupin Ltd., Lupin Pharmaceuticals, Inc. Also represented by PAUL J. MOLINO, DEANNE M. MAZZOCHI, THEODORE JOSEPH CHIACCHIO, JOHN POLIVICK.

STEVEN D. ROTH, Locke Lord, LLP, New York, NY, argued for defendant-appellant Hi-Tech Pharmacal Co., Inc. Also represented by THOMAS J. VETTER, Lucas & Mercanti, LLP, New York, NY.

Before LOURIE, LINN, and HUGHES, *Circuit Judges.*

LOURIE, *Circuit Judge.*

Sandoz Inc. ("Sandoz"), Lupin Ltd. and Lupin Pharmaceuticals, Inc. (collectively, "Lupin"), and Hi-Tech Pharmacal Co., Inc. ("Hi-Tech") (collectively, "the Appellants")[1] appeal from the decision of the United States District Court for the Eastern District of Texas, following a bench trial, which held that the claims of U.S. Patents 7,851,504 (the "'504 patent"), 8,278,353 (the "'353 patent"), 8,299,118 (the "'118 patent"), 8,309,605 (the "'605 patent"), and 8,338,479 (the "'479 patent"), asserted by Allergan, Inc. ("Allergan"), were not shown to be invalid for obviousness under 35 U.S.C. § 103, and that the

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[1] Watson Laboratories, Inc., Watson Pharmaceuticals, Inc., and Watson Pharm, Inc. (collectively, "Watson") were also defendants-appellants initially. But Watson has since been dismissed from this appeal on a joint motion filed by Watson and Allergan. *See Allergan, Inc. v. Sandoz Inc.*, No. 14-1275, ECF No. 121 (Fed. Cir. Apr. 17, 2015).

claims of the '353 and '118 patents were not shown to be invalid for lack of an adequate written description under 35 U.S.C. § 112, ¶ 1.[2] *Allergan, Inc. v. Sandoz Inc.*, No. 6:11-cv-00441, ECF No. 303, slip op. at 77, 79 (E.D. Tex. Jan. 13, 2014) ("*Opinion*"). Additionally, Lupin challenges the district court's determination that the claims of Allergan's patents were not shown to be invalid for lack of enablement under § 112, ¶ 1. *Id.* at 80–81. Hi-Tech also challenges the district court's finding that it infringed the claims of the '504, '605, and '479 patents literally and under the doctrine of equivalents. *Id.* at 64–66. For the reasons that follow, we *affirm* in all respects.

BACKGROUND

I

Glaucoma is an eye disease associated with elevated intraocular pressure ("IOP"). Treatments that effectively reduce IOP can slow the progression of the disease. If left untreated, however, elevated IOP can damage the optic nerve and lead to permanent vision loss and blindness. In 2001, the U.S. Food and Drug Administration (the "FDA") approved Lumigan® 0.03% ("Lumigan 0.03%"), a once-daily topical solution developed by Allergan, for treating open angle glaucoma and ocular hypertension. Lumigan 0.03% contains 0.03% by weight of bimatoprost and 50 parts per million ("ppm") benzalkonium chloride ("BAK"), among other ingredients.

Bimatoprost, the active ingredient in Lumigan 0.03%, is a prostaglandin analog that effectively lowers IOP, but can cause hyperemia, *i.e.*, red eye, when administered to

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[2] Because the applications resulting in the patents asserted in this case were filed before the enactment of the Leahy-Smith America Invents Act ("AIA"), Pub. L. No. 112-29, 125 Stat. 284 (2011), we apply the pre-AIA version of 35 U.S.C. § 103 and § 112.

the ocular surface. One structural difference between bimatoprost and two other prostaglandin analogs that were approved for treating glaucoma at the time of its approval, Xalatan® (latanoprost) and Travatan® (travoprost), is that bimatoprost contains an amide, instead of an ester as in latanoprost and travoprost. *Opinion* at 7–8. It was understood that both latanoprost and travoprost, but not bimatoprost, act as prodrugs of the corresponding acids. *Id.*

BAK is a preservative for inhibiting bacterial growth in ophthalmic solutions. It was known, however, that BAK is cytotoxic and that it can damage the cells on the ocular surface and cause undesirable side effects.

Although Lumigan 0.03% was effective at lowering IOP, it also caused frequent and severe hyperemia. Many patients thus stopped using it without consulting their physicians, which led to gradual vision loss. To address that problem, Allergan explored a number of alternative formulations of bimatoprost and surprisingly discovered that increasing the concentration of BAK from 50 ppm to 200 ppm significantly increased the corneal permeability of bimatoprost. *Id.* at 12–13. After further research, Allergan developed Lumigan® 0.01% ("Lumigan 0.01%").

Lumigan 0.01% is a topical solution containing 0.01% bimatoprost and 200 ppm BAK; otherwise, it has the same ingredients as Lumigan 0.03%. Thus, as compared with Lumigan 0.03%, Lumigan 0.01% has a three-fold lower bimatoprost concentration and a four-fold higher BAK concentration. Clinical studies showed that Lumigan 0.01% has similar efficacy to Lumigan 0.03%, *viz.*, IOP-lowering within 0.5 mmHg of that of Lumigan 0.03%, but it causes less frequent and severe hyperemia than Lumigan 0.03%. *Id.* at 20–21. In 2010, the FDA approved Allergan's New Drug Application for Lumigan 0.01% for the same approved uses as Lumigan 0.03%.

II

Allergan owns the '504, '353, '118, '605, and '479 patents, which are all listed in the FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations* (commonly known as the "Orange Book") as claiming Lumigan 0.01% and its approved uses. After Allergan received FDA-approval of Lumigan 0.01%, Sandoz, Lupin, Hi-Tech, and Watson each submitted an Abbreviated New Drug Application ("ANDA") to the FDA, seeking approval to engage in the commercial manufacture, use, importation, sale, or offer for sale of generic versions of Lumigan 0.01% prior to the expiration of the '504, '353, '118, '605, and '479 patents. In response, Allergan sued each of the ANDA applicants in the United States District Court for the Eastern District of Texas, asserting that their ANDA filings infringed those patents. The district court consolidated those actions into one case.

The asserted patents all derive from an application filed on March 16, 2005 and share a common specification. The patents are entitled "Enhanced Bimatoprost Ophthalmic Solution," '504 patent col. 1 ll. 1–2,[3] and refer to what is Lumigan 0.03% in the background section, *id.* col. 1 ll. 34–36. The specifications of the patents describe a composition comprising 0.005% to 0.02% bimatoprost and 100 ppm to 250 ppm BAK, which is an aqueous liquid "formulated for ophthalmic administration" and "useful in treating glaucoma or ocular hypertension." *Id.* col. 1 ll. 61–67. The specifications also specifically describe a formulation comprising *0.01%* bimatoprost and *200 ppm* BAK, among other formulations, as a "best mode" of the invention. *Id.* col. 2 ll. 59, 64–67.

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[3] Because the asserted patents share an identical specification in relevant part, we refer only to the '504 patent when discussing the specifications of those patents.

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